REMARKS/ARGUMENTS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

The claims have been revised to define the invention with additional clarity. Claims 49 and 52 have been cancelled without prejudice.

Rejections Under 35 USC 112, second paragraph

The term 'antagonised' has been replaced by 'wholly or partially reversed' in claims 50 and 53.

The antecedent basis of the term 'heterologous nucleic acid' has been revised in claims 59 and 69.

Claims 61 and 63 are now dependent on claim 59.

In the light of the above, reconsideration of the rejection of claims 50, 53, 55-58, 68 and 69 and the rejection of claims 61-67 is requested.

Rejection of claims 49, 52-59 and 61-69 under 35 USC 112, first paragraph (written description).

Claims 49 and 52 have been cancelled, rendering moot rejections thereof.

Claims 53 and 54 have been amended to specify that the polypeptides contain the 17 amino acid gibberellin interaction domain.

All the claimed nucleic acids encode proteins having the same activity as SEQ ID NO:2.

As described below, the hybridization conditions in claims 53 and 54 are from Peng et al, Plant Cell (1993) 5:351-360, which is incorporated into the specification by reference (page 33, lines 5-6). Further, the present application claims a priority date in 1998, which is 5 years after the publication date of the Peng reference. One of skill in the art at the time of filing would have been well aware of the appropriate hybridization conditions that could be used as currently claimed.

The written description requirement has therefore been met for the current claims and reconsideration of the rejection is requested.

Rejection of claims 52-59 and 61-69 under 35 USC 112, first paragraph (written description).

The Examiner asserts that the hybridization conditions in claims 52-54 add new matter.

Claim 52 has been cancelled, rendering moot rejections thereof.

As mentioned above, the hybridization conditions recited in claims 53 and 54 are taken from Peng et al which is listed as reference 5 on page 48 of the specification. This paper is incorporated into the specification by reference on page 33, lines 5-6. Also, as stated above, the present application claims a priority date in 1998, which is 5 years after the publication date of the Peng reference. One of skill in the art at the time of filing would have been well aware of the appropriate hybridization conditions that could be used as currently claimed.

In the light of this, the recited hybridization conditions do not constitute added matter and claims 53 and 54, and claims dependent thereon, are allowable. Reconsideration of the rejection is requested.

Rejection of claims 49-59 and 61-69 under 35 USC 112 first paragraph (enablement)

The Examiner considers that the specification does not enable isolated nucleic acids encoding a polypeptide that has 90% identity to SEQ ID NO:2 and which comprises the 17 amino acid sequence underlined in Figure 4, and other related aspects of the invention.

In view of the teaching of the specification, the skilled person would have no difficulty in making and using nucleic acids which fall within the present claims. All nucleic acids within the claimed genus have the function of causing gibberellin sensitive dwarfism. The skilled person would be readily able to determine the presence or absence of a dwarf phenotype and whether this phenotype is affected by gibberellin. For example, the use of gibberellin to treat plants is described on page 6, lines 1 to 14, of the specification. Furthermore, the claimed sequences are closely related by structure to the reference sequence. This close relationship allows the experimentation required to confirm activity in the manner taught by the specification to be minimized. This level of experimentation is not undue.

In particular, given the teaching of the specification, a skilled person would have no difficulty in identifying sequences which are closely related to the reference sequence (i.e. have at least 90% sequence identity), possess the claimed activity and contain the

specific 17 amino acid region. This region is taught by the specification to be responsible for gibberellin interaction. Following the guidance set out in the specification, the skilled person can test a polypeptide for ability to confer a gibberellin responsive dwarf phenotype using methods which are routine in the art. In determining whether this amount of experimentation is undue, *in re Wands* sets out various factors which must be considered. For the reasons set out below, consideration of these factors shows any experimentation required by the skilled person in working the claimed invention is not undue and the disclosure of the specification therefore meets the requirements of 35 USC §112, first paragraph.

a) The nature of invention/scope of claims

The claimed invention relates to isolated nucleic acid sequences the expression of which in a plant confers gibberellin sensitive dwarfism. The polypeptide can be a GAI sequence which shares 90% sequence identity with SEQ ID NO:2 and which comprises the 17 amino acid gibberellin interaction domain. The isolated nucleic acid can, for example, hybridize under specified highly stringent conditions with the sequence encoding SEQ ID NO: 2.

The genus of nucleic acids covered by these claims is narrow and defined according to a close structural relationship to SEQ ID NO: 2. The sequence of SEQ ID NO: 2 thus defines and limits the structure of all the members of the genus. The genus is further defined by the specific function of conferring gibberellin insensitive dwarfism on a plant.

The invention thus concerns a group of nucleic acid molecules encoding polypeptides which have a close structural relationship (at least 90% sequence identity) and which possess a common activity.

b) Predictability of the art

The techniques of protein engineering are well established in the art and a skilled person can reliably modify a protein sequence as required without difficulty.

Furthermore, a skilled person is aware of the properties of different amino acid residues and can identify important positions within the polypeptide sequence by routine sequence analysis. The skilled person can thus by and large predict whether or not a particular sequence change will disturb protein function without undertaking any experimentation.

c) Quantity of experimentation necessary

DNA manipulation, cloning and hybridization techniques and assays for testing whether a polypeptide has GA-responsive dwarfing activity are routine in the art.

The repetition of such routine techniques does not put them beyond the level of one skilled in the art. If they are routine, the skilled person can perform them any number of times without intellectual or creative input. It is noted that '*a considerable amount of experimentation is permissible, if it is merely routine.*'(*In re Wands*).

Furthermore, the skilled person is not required to undertake an extensive synthesis and screening program covering every conceivable nucleic acid that might be

encompassed by the claims. Given the narrow genus of isolated nucleic acids encompassed by the claims, there is a reasonable expectation that most if not all nucleic acids which possess the structural features will have the claimed activity. The skilled person will need to test very few hybridizing nucleic acids in order to identify a nucleic acid with the stated activity. The level of experimentation required to test these few nucleic acids using routine techniques is not undue.

d) Relative skill of those in the art

A person skilled in the field of plant molecular biology at the filing date would have a high level of skill and experience in the manipulation of DNA and the cloning and expression of plant genes.

The skilled person would also be familiar with known methods of testing for gibberellin responsiveness and dwarf phenotypes.

Thus, the skilled person would be experienced in all the techniques which would be required to carry out the claimed invention.

e) <u>Amount of guidance provided by the inventors</u>

Contrary to the Examiner's assertion, there is significant guidance in the specification for the skilled person to practice the invention.

Variants and homologues of the sequence of Figure 4 are discussed in detail in the specification, for example, on page 6, line 25 to page 7, line 14 and page 17, line 1 to page 19, line 7. The specification teaches the skilled person how to identify variant

sequences in terms of % identity using sequence analysis software from page 16, line 3 to page 16, line 20 and how to identify variant sequences in terms of hybridization to the reference sequence under stringent conditions from page 12, line 19 to page 14, line 20. Page 11, line 18 to page 12, line 13 also teaches the use of antibodies to identify GAI homologues.

Guidance on the cloning and manipulation of GAI variant nucleic acid sequences is provided by the specification on page 7, line 15 to page 10, line 21 and page 23, line 11 to page 25, line 22. Further guidance on the transformation of cells with GAI nucleic acid sequences and the production of transgenic plants is provided on page 25, line 23 to page 30, line 2 of the specification. A hypothetical example of the cloning and testing of variant sequences is provided on page 45, line 24 to page 46, line 18.

The skilled person is readily able to determine the activity of an isolated nucleic acid in a plant by assessing whether or not a dwarf phenotype is produced and whether or not this phenotype is sensitive to gibberellin, i.e., whether or not the plant will revert to wild-type on treatment of the plant with gibberellin. The use of gibberellin is discussed in the specification on page 4, line 15 to page 6, line 14.

In the light of the above it is clear that the directions provided by the inventors in the specification provide ample guidance to allow persons skilled in the art to work the invention as claimed.

f) Existence of worked examples

The specification exemplifies the identification of the GAI gene and the mutant gai gene in Arabidopsis on page 34, line 25 to page 42, line 9. Further examples of the manipulation and expression of GAI and gai nucleic acid sequences are provided on pages 43, line 22 to page 45, line 20. A hypothetical example of the cloning of Gai homologues is described on page 42, line 14 to page 43, line 19. The results of EST database screening for GAI homologues are shown in Table 2. Worked examples of the invention are, therefore, provided in the specification.

In summary, an analysis of the factors set out in *In re Wands* indicates that no undue experimentation would be required by one skilled in the art to make and use the claimed invention. Claims 49 to 70 are fully enabled by the present specification and meet the requirements of 35USC§112, first paragraph (enablement). Reconsideration of the rejection is respectfully requested.

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

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Respectfully submitted,

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